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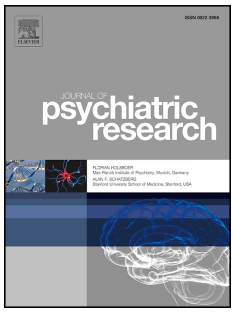

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A population study of the association between sleep disturbance and suicidal behaviour in people with mental illness

Journal of Psychiatric Research

Running title: Sleep and suicide in mental illness

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Conflict of interest

BS, YTW, MP, YL, TDC declare they have no direct conflict of interest

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Abstract (word count 243/250)

Limited representative research has considered the relationship between sleep disturbance and suicidal behaviour among people with mental illness. We investigated the relationship between sleep disturbance and suicidal behaviour across Part II interview of the National Comorbidity Survey Replication (NCSR). The associations between sleep disturbance and suicidal behaviour (thoughts, plans and attempts) were investigated using logistic and multinomial logistic regressions and stratified across six mental disorder groups (depression, anxiety, substance use disorders (SUD), eating disorders (ED), bipolar disorders (BD) and early life disorders). From 5,701 participants (mean age 43.4 years 58% women), people with any mental disorder experiencing sleep disturbance were at increased odds of suicidal thoughts (odds ratio (OR): 2.5; 95% CI: 1.7, 3.6) and suicidal plans and attempts (OR: 5.7; 95% CI: 2.7, 11.9) adjusting for age, sex and income. People with BD (OR: 8.9; 95 CI: 2.1, 38.1), early life disorders (OR 6.98, 95% ci 2.48, 19.67), depression (OR 1.88, 95% CI 1.14, 3.11), anxiety (OR 1.90, 95% CI 1.28, 2.85) and SUD (2.60, 95% CI 1.23, 5.49) but not ED, were at increased odds of suicidal thoughts in the presence of sleep disturbance. Adjusting for anti-depressant intake attenuated the effect sizes by up to 20% but the associations remained significant. In conclusion, sleep disturbance is a potential risk factor for suicidal behaviours in people with mental illness. Monitoring and management of sleep disturbance in clinical practice might be an important strategy to mitigate suicidal behaviours in people with mental illness.

Key words: Suicide; Sleep disturbance; Mental disorders; mental illness, sleep, schizophrenia, bipolar disorder, suicidal

Introduction

Suicide is a pervasive, but preventable, cause of death, affecting both sexes, all races, people across the socioeconomic status spectrum and throughout the lifespan (Nock *et al.*, 2008). Globally, there are over a million deaths by suicide each year (Krug *et al.*; Wilcox and Wyman, 2016).Suicide remains a leading cause of death among people below the age of 40 (Mcloughlin *et al.*, 2015). The negative implications of suicide extend beyond the individual to families, communities, caregivers and health care providers. Consequently, the prevention of suicidal behaviour is a global priority.

In the US, suicide is the 10th leading cause of death with approximately 30,000 deaths annually (Goldsmith and Institute of Medicine (U.S.). Committee on Pathophysiology & Prevention of Adolescent & Adult Suicide.; Murphy *et al.*). These statistics do not include rates of suicidal ideation and attempts, which greatly outnumber completed suicides; between 10-25 nonlethal suicide attempts are made for each lethal suicide attempt (Maris, 2002). There is evidence of a clear escalation from suicidal ideation, plans and attempts, with a recent study across 17 countries demonstrating that 60% of people transition from ideation to attempts within one year (Nock *et al.*, 2008). Thus, the identification and management of risk factors at an early stage is key and the prevention of the spectrum of suicidal behaviours is essential.

Recently, interest has begun in the relationship between poor sleep and mental illness (Steinan *et al.*, 2015; Cho *et al.*, 2016; Sheaves *et al.*, 2016), the onset of pain (Bonvanie *et al.*, 2016) and burnout (Grossi *et al.*, 2015) all of which are also associated with suicidal behaviours (Wilcox and Wyman, 2016). Surprisingly, despite the established bidirectional relationship between sleep disturbances and depression, (Lustberg and Reynolds, 2000) and mental illness and suicide (Harris and Barraclough, 1997), a paucity of research has considered the

relationship between sleep difficulties and suicidal behaviours among people with recognised mental illnesses. Whilst a previous study (Wojnar *et al.*, 2009) found that the relationship between sleep disturbance and suicide remained robust after the adjustment for mental illness diagnosis, there is growing interest in the specific risk of sleep and suicide among people with established mental illnesses. A previous meta-analysis found across 13 studies that sleep disturbance was associated with a range of suicidal behaviours in people with depression/ depressive disorder (Malik et al., 2014). However, very few of the included studies were drawn from representative samples (i.e. sample sizes >2,000) and the authors found a paucity of studies considering this relationship in other mental illnesses. For instance, the relationship between sleep disturbance and suicide in people with schizophrenia, affective disorder and panic disorder are limited to evidence drawn from single studies, therefore, clearly precluding any definitive conclusions. Very little research appears to have considered the relationship between sleep disturbance and suicidal behaviour among people with other mental illness classifications such as bipolar disorder, substance use disorder and eating disorders.

Given that a) mental illness is often a central risk factor for suicidal behaviour (Haw and Hawton, 2015), b) sleep disturbances are common among people with mental illness (Ohayon, 1997) and c) sleep disturbances are an established risk factor for suicide among people without mental (Bernert and Nadorff, 2015), it is important to consider if sleep disturbances are associated with suicidal behaviour in people with mental illness. Understanding if sleep disturbance is a risk factor for suicidal ideation could be important for clinical practice, research and policy.

The aim of this study is to investigate the associations between suicidal behaviour and sleep disturbance in people with and without mental disorders across a representative cohort of US adults. In particular, we sought to investigate if the risk of suicidal behaviour differed among those with different mental illness classifications.

Methods

Study population

The analysis was based on the Part II subsample of the National Comorbidity Survey Replication (NCSR). The NCSR is a part of the Collaborative Psychiatric Epidemiological Surveys (CPES), together with the National the National Latino and Asian-American Survey (NLAAS) and the National Study of American Life (NSAL). These three surveys were carried out by the professional interviewers using the same diagnostic instrument during the same time period. The primary objective of the CPES was to collect data about the prevalence of mental disorders, their associated impairments and treatment patterns from representative samples of majority and minority adult populations in the US (http://www.icpsr.umich.edu/icpsrweb/ICPSR/studies/20240).

The NCSR Part II interview was administered to participants reporting with a lifetime mental disorder in the Part I survey and a probability subsample of other participants without a lifetime mental disorder. More detailed information on sampling methods and ethical approval including the committee number is detailed elsewhere (Kessler *et al.*, 2004). This study included 5701 people who answered questions related to sleep disturbance in the past 12 months.

Mental illness classification

All mental illnesses were based on the DSM-IV diagnoses in the CPES. Subsequently, participants were divided into six groups of mental disorders based on the last 12 months including depression, anxiety, substance related disorders (alcohol, drug and nicotine), early life disorders (usually first diagnosed in infancy, childhood or adolescence), eating disorders and bipolar disorders.

Suicidal behaviour

Suicidal behaviour in the past 12 months was defined using self-reported information on suicidal thoughts, plan and attempt. Since suicidal thoughts were more frequent than suicidal plans or attempts, a binary variable was generated to identify those with or without suicidal thoughts in the past 12 months. In addition to suicidal thoughts, a measure of suicidal levels further considered those reporting suicidal plan or attempt and categorised the study population into three groups: no suicidal in the past 12 months, suicidal thoughts only, suicidal plan or attempt. There was a small number of people who had suicidal plan or attempt but no suicidal thoughts (N=16).

Sleep disturbance

The measures of sleep disturbance included three symptoms in the past 12 months: taking 2 or more hours to fall asleep for more than 2 weeks ('Did you have a period lasting two weeks or longer in the past 12 months when nearly every night it took you two hours or longer before you could fall asleep?'), taking 1 or more hours to get back to sleep for more than 2 weeks ('Did you have a period lasting two weeks or longer in the past 12 months when you woke up nearly every night and took an hour or more to get back to sleep?') and feeling sleepy during the day for more than 2 weeks ('Did you have a period lasting two weeks or longer in the past 12 months when you had problems feeling sleepy during the day?') woke up nearly every morning at least two hours). Those who reported any of these symptoms were considered to have sleep disturbance.

Covariates

Socio-demographical variables including age, sex and income to need ratio was considered to be potential confounding factors for the associations between suicidal behaviour and sleep

disturbance. The measure of income to need ratio in CPES was based on the US Census 2001 with a scale between 0 and 17. Ratios below 1 indicate that the income for individuals was below the official definition of poverty. Anti-depressants were common treatments for mental disorders (Sharma *et al.*, 2016). The self-reported intake of anti-depressants might mitigate psychiatric symptoms and reduce suicidal behaviour (Mann *et al.*, 2005).

Analysis

Logistic regression was used to investigate the associations between suicidal thoughts and sleep disturbance in the total population and the interaction terms of sleep disturbance and any mental disorders adjusting for age, sex, income and anti-depressant intake. The associations between suicidal levels and sleep problems were examined using multinomial logistic regression to estimate the odds ratios for three suicidal levels. Although the estimates from multinomial logistic regression were relative risk ratio (RRR), they should be interpreted as odds ratio in this cross-sectional study. To investigate the potential differential relationships across mental disorder subgroups, the associations between suicidal behaviour and sleep disturbance were stratified by mental disorder group and the six subgroups.

Results

Participant details

In total, there were 5,701 participants included within the current study with a mean age of 43.4 years (standard deviation=16.6) and 58% were women (Table 1). Among the total participants, 50.5% (N=2876) reported sleep disturbance in the past 12 months and 46.5% (N=2654) had a mental disorder in the past 12 months. There were 144 (2.5%) people reporting suicidal thoughts in the past 12 months and 91 (1.6%) having suicidal plans or attempts regardless of suicidal thoughts. Lower prevalence of suicidal behaviour was found in those without mental disorders (0.8%) and those without sleep disturbance (1.8%) compared to their counterparts.

Insert table 1 here

Suicidal behaviours among people with sleep disturbance

Table 2 reports unadjusted and adjusted odds ratios of suicidal thoughts among people with and without sleep disturbance. People reporting sleep disturbance had a 3.5 times higher odds (OR: 3.5; 95% CI: 2.6, 4.9) of having suicidal thoughts compared to their counterparts, after adjusting for age, sex and income. Compared to people who did not have any mental disorders and sleep disturbance in the past 12 months, people with mental disorders had nearly 6 times higher odds (OR: 5.8; 95% CI: 3.0, 11.1) of having suicidal thoughts and those also reporting sleep disturbance had 14.6 times higher odds (OR: 14.6; 95% CI: 8.1, 26.3). However, the interaction term of mental disorders and sleep disturbance did not achieve statistical significance (p-value=0.22). After further adjusting for anti-depressant intake, the odds ratios in mental disorder group were attenuated to 4.8 (95% CI: 2.5, 9.3) for those without sleep disturbance and 10.4 (95% CI: 5.7, 18.9) for those with sleep disturbance.

Insert table 2 here

Sleep disturbance and suicidal behaviour among people with and without mental illness

The associations between suicidal thoughts and sleep disturbance were different in people with and without mental disorders (Table 3). In the non-mental disorder group, sleep disturbance was associated with a non-significant 1.5 times (OR: 1.5; 95% CI: 0.7, 3.5) higher odds of suicidal thoughts, while in the mental disorder group, the odds ratio was significant and increased to 2.5 (OR: 2.5; 95% CI: 1.7, 3.6) after adjusting for socio-demographic factors. Further controlling for anti-depressant intake slightly attenuated the effect size, but the association remained statistically significant in people with any mental disorders (OR: 2.1; 95% CI: 1.5, 3.1). The associations varied across different mental disorder subgroups with a range of odds ratio from 2.2 (95% CI: 1.3, 3.6) for depression to 8.9 (95% CI: 2.1, 38.1) for bipolar disorders.

Insert table 3 here

Table 4 reports the association between sleep disturbance and suicidal thoughts, plans and attempts. For those who had any mental disorder, sleep disturbance was associated with almost 6 times (OR: 5.7; 95% CI: 2.7, 11.9) higher odds of suicidal plans or attempts while the association was unclear in non-mental disorder group. Similar effect sizes were found in the subgroups of depression (OR: 4.0; 95% CI: 1.7, 9.5) and anxiety (OR: 5.2; 95% CI: 2.4, 11.5). Further adjusting for anti-depressant intake attenuated the strength of the associations by up to 20%.

Insert table 4 here

Discussion

This study investigated the association between sleep disturbance and suicidal behaviour in US adults with and without mental disorders. For people with mental disorders, sleep disturbance was associated with increased odds of suicidal thoughts (OR: 2.5; 95% CI: 1.7, 3.6) and suicidal plans and attempts (OR: 5.7; 95% CI: 2.7, 11.9) after adjusting for age, sex and income. An increase in odds of suicidal behaviour was noted across all mental disorders in individuals who experienced sleep disturbances, however, a particularly strong relationship was found in individuals with bipolar disorders (OR: 8.9; 95 CI: 2.1, 38.1). Further, adjusting for anti-depressant intake attenuated the effect sizes by up to 20% but all of the associations remained statistically significant.

Our results highlight that people with mental disorders and sleep disturbance are at particularly increased odds of experiencing suicidal behaviour. Our data build upon the previous, scant literature in several ways. First, very few representative cohort studies (n>2,000) have been conducted investigating sleep disturbance and suicidal behaviour among people with mental illness. For instance, a previous review (Malik et al., 2014) identified only three studies (Paffenbarger et al., 1994; Nrugham et al., 2008; Bjorngaard et al., 2011) with over 2,000 participants included in their sample sizes that have investigated this issue. Moreover, each of these previous representative cohort studies was limited to investigations of depression/ anxiety, and two solely focussed on suicide completion (Paffenbarger et al., 1994; Bjorngaard et al., 2011). Given that the identification of earlier suicidal behaviours is integral to prevent an escalation in suicidal behaviours (Mann *et al.*, 2005), our data identifying

the increased risk of suicidal thoughts and behaviours in those with mental illness is important. Second, we have expanded the scope of previous investigations on depression/anxiety to include eating disorders, bipolar disorders, substance use and early life disorders. To our knowledge, only one prior study (n=90) has investigated sleep disturbance and eating disorders (Mayes *et al.*, 2014), with the authors suggesting potential relationship. In our study, we did not observe a relationship between sleep and suicidal ideation in eating disorder, which may be due to a lack of power given that we only had 90 participants in this analysis. The relationship between sleep disturbance and affective disorders is also unclear. A previous review (Malik *et al.*, 2014) identified only one previous study among people with affective disorders. This breakthrough study (Fawcett *et al.*, 1990) included people with 569 people with unipolar depression, 185 bipolar disorder I, 114 bipolar disorder II and 80 people with schizoaffective disorder. However, the paper was published over 25 years ago (Fawcett *et al.*, 1990) and did not disentangle the individual diagnostic relationships with suicidal behaviour. Our data on bipolar disorder indicates that this population are at particular increased risk of suicidal behaviour when sleep disturbance is present. This is an important finding given that sleep disturbance is common in this population across all phases of the illness and associated with deteriorating mental health (Plante and Winkelman, 2008). Our findings, add to the growing recognition of the importance of managing sleep in this population. Our results also align with a systematic review by Malik et al (2014) which identified in 13 studies that sleep disturbance is associated with increased risk of suicidal behaviour in people with depression.

Our analyses also demonstrate that the adjustment for antidepressant medication does appear to ameliorate the association between sleep disturbance and suicide in people with mental illness. In particular, there was a narrowing of the confidence intervals for the

relationship in people with BD. There has previously been considerable debate regarding the influence of antidepressant and suicidal behaviour (Healy and Whitaker, 2003; Sharma *et al.*, 2016). Our data suggest that antidepressant medication may offer a slight protective effect for suicidal behaviour in people with mental illness, although the observational nature of these data precludes any definitive conclusions. However, the exact potential mechanism of this relationship is not yet fully elucidated and future research (including qualitative research) should consider this important question.

Our findings strengthen and widen the evidence base that sleep disturbance is a potential risk factor for suicidal behaviours in people with mental illness. Clinicians treating people with mental illness should be aware that changes in sleep pattern and in particular difficulty getting to sleep may elevate a person's risk of suicidal ideation. Therefore, clinicians may consider asking additional questions about sleep disturbance to aid their suicidal risk assessment, including comprehensive details about sleep quality, duration and daytime function. Appropriate interventions to address sleep difficulty should be a priority among people with mental illness. Further studies are needed to identify sleep interventions specifically targeted at patients with mental illness.

Limitations

Some important limitations should be considered in the interpretation of these findings. First, some of the mental illness classifications included relatively few participants, and we could not investigate the relationships in people with psychosis as there was no diagnosis on these classifications. In addition, whilst we found particularly high odd ratios for bipolar and early life disorders, their confidence intervals, due to small sample size, were very broad and suggest uncertainty of point estimates. Therefore, future studies with larger number of patients and

more categories of mental illness are warranted. Second, some physical comorbidity might cause sleep disturbance and suicidal behaviour and could have potential confounding effects on the associations. However, we did examine a wide range of chronic conditions (chronic pain, arthritis, frequent and severe headache, back/neck problems) but these were not associated with suicidal behaviour. Third, the analysis was based on the NCSR Part II interview, which is a subsample focusing on people reporting a mental disorder in Part I and a proportion of the rest of the original sample. This might have led to the absence of an unclear association between sleep disturbance and suicidal behaviour in the non-mental disorder group. Fourth, we did not adjust for severity of mental health symptoms (e.g. depressive symptoms) which could moderate the associations we observed, since the information was not available. Finally, since this is a cross-sectional study, the associations found in the analysis cannot indicate causal relationships between sleep disturbance, mental illnesses and suicidal behaviour. Although our hypothesis was that sleep disturbance might be a risk factor for suicidal behaviour, the direction could be reversed given their strong relationship. In addition, sleep disturbance was captured with a measure covering a two week period in the past 12 months. Future longitudinal research would be useful to attempt to disentangle these relationships and should seek to utilise more rigorous and in-depth questions regarding sleep disturbance (covering a longer time period) and suicidal behaviours.

Nonetheless, allowing for the aforementioned caveats, our data offer novel insight into the potential hazard of sleep disturbance on suicidal risk in people with established mental illness. Future prospective research is required to confirm our findings.

Conclusion

This study suggests that sleep disturbance is a potential risk factor for suicidal behaviour particularly in people with mental disorders. Changes in sleep patterns should receive more attention in clinical practice and future research in order to develop possible interventions on suicide prevention. Future representative longitudinal research is required to further understand the relationships between sleep disturbance and suicidal behaviour in people with mental illness. Such research should consider these relationships in substance use disorders, bipolar disorders and eating disorders and seek to use measures which capture sleep disturbance over a longer period of time.

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Table 1 Descriptive information on socio-demographics and mental disorders

	Suicidal behaviour		Total
	Thoughts (N=144, 2.5%)	Plans and attempts (N=91, 1.6%)	(N=5701)
Age (mean, std.)	38.2 (14.6)	35.0 (12.1)	43.4 (16.6)
Sex (% women)	67.4%	60.4%	58.1%
Income to need ratio (mean, std.)	3.3 (3.0)	3.0 (3.4)	4.5 (3.8)
Sleep problems (N, %)			
Yes	106 (3.7)	79 (2.8)	2876
No	38 (1.4)	12 (0.4)	2825
Non mental disorders	17 (0.6)	6 (0.2)	3047
Mental disorders in the past 12 months (N, %)			
Any mental disorders	127 (4.8)	85 (3.2)	2654
Depression	84 (8.9)	69 (7.3)	946
Anxiety	106 (5.3)	76 (3.7)	1993
Substance use disorders	33 (6.1)	26 (4.8)	541
Eating disorders	5 (5.6)	8 (8.9)	90
Bipolar disorders	23 (8.9)	26 (10.4)	259
Early life disorders	45 (6.9)	40 (6.2)	648

Table 2 Unadjusted and adjusted odds ratio of suicidal thoughts in the past 12 months among people with and without sleep disturbance (logistic regression)

	Model 1		Model 2		Model 3		Model 4	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Age	0.97	(0.96, 0.98)	0.97	(0.96, 0.98)	0.98	(0.97, 0.99)	0.98	(0.97, 0.99)
Sex (female vs male)	**1.45**	(1.18, 1.77)	1.08	(0.82, 1.44)	0.99	(0.74, 1.32)	0.83	(0.62, 1.11)
Income	0.91	(0.88, 0.94)	0.90	(0.85, 0.94)	0.91	(0.86, 0.95)	0.90	(0.86, 0.95)
Anti-depressant							**3.75**	(2.78, 5.04)
No sleep disturbance	1.00	reference	1.00	reference	1.00	reference	1.00	reference
Sleep disturbance	**3.66**	(2.66, 5.03)	**3.53**	(2.57. 4.88)	1.42	(0.61, 3.29)	1.32	(0.57, 3.08)
Any mental disorders					**5.77**	(2.99, 11.14)	**4.82**	(2.49, 9.34)
Sleep disturbance + any mental disorders					**14.56**	(8.05, 26.34)	**10.38**	(5.69, 18.93)

Model 1: Univariate model; Model 2: Adjusted for age, sex and income; Model 3: Interaction terms of sleep disturbance and mental disorders adjusted for age, sex and income; Model 4: Model 3 further adjusted for anti-depressant; **Bold:** odd ratio achieved statistical significance

Table 3 Unadjusted and adjusted odds ratio of suicidal thoughts in the past 12 months among people with and without sleep disturbance by different mental disorder subgroups (logistic regression)

	Model 1		Model 2		Model 3	
	OR	95%CI	OR	95%CI	OR	95%CI
No mental disorders	1.40	(0.60, 3.24)	1.50	(0.65, 3.52)	1.43	(0.61, 3.37)
Any mental disorders	**2.48**	(1.73, 3.56)	**2.50**	(1.74, 3.60)	**2.13**	(1.47, 3.08)
Depression	**2.06**	(1.27, 3.36)	**2.17**	(1.33, 3.56)	**1.88**	(1.14, 3.11)
Anxiety	**2.22**	(1.50, 3.28)	**2.22**	(1.50, 3.30)	**1.90**	(1.28, 2.85)
Substance use disorders	**2.97**	(1.42, 6.19)	**2.87**	(1.37, 6.03)	**2.60**	(1.23, 5.49)
Eating disorders	2.84	(0.34, 23.64)	3.14	(0.36, 27.32)	1.10	(0.19, 11.86)
Bipolar disorders	**9.09**	(2.14, 38.64)	**8.87**	(2.06, 38.13)	**7.62**	(1.72, 33.66)
Early life disorders	**8.58**	(3.09, 23.82)	**7.85**	(2.81, 21.87)	**6.98**	(2.48, 19.67)

Model 1: Univariate model; Model 2: Adjusted for age, sex and income; Model 3: Adjusted for age, sex, income and anti-depressant; **Bold:** odds ratio achieved statistical significance

Table 4 Adjusted odds ratio of suicidal thoughts, suicidal plan or attempt in the past 12 months among people with and without sleep disturbance by different mental disorders (multinomial logistic regression)

	Model 1				Model 2			
	Suicidal thoughts		Suicidal plan or attempt		Suicidal thoughts		Suicidal plan or attempt	
	RRR	95%CI	RRR	95%CI	RRR	95%CI	RRR	95%CI
No mental disorders	2.02	(0.77, 5.29)	0.90	(0.16, 5.01)	2.04	(0.78, 5.35)	0.76	(0.13, 4.35)
Any mental disorders	**1.78**	(1.17, 2.71)	**5.72**	(2.74, 11.94)	**1.60**	(1.04, 2.44)	**4.55**	(2.16, 9.58)
Depression	1.54	(0.86, 2.78)	**4.02**	(1.70, 9.50)	1.41	(0.78, 2.56)	**3.30**	(1.38, 7.88)
Anxiety	1.54	(0.98, 2.43)	**5.22**	(2.37, 11.50)	1.39	(0.88, 2.21)	**4.26**	(1.91, 9.51)

Model 1: Adjusted for age, sex and income; Model 2: Adjusted for age, sex, income and anti-depressant;

Bold: odds ratio achieved statistical significance

Contributors

All authors conceived the study, YTW, TDC analysed the data, BS, YTW wrote the manuscript, all authors have read and approved the final version.